Updates on Canine Atopic Dermatitis

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“If he keeps scratching,” said Emily Elizabeth’s dad, “he will have to go to the vet.”

The vet? thought Clifford.

Clifford had never been to the new vet before.

- Itching is a PAIN
- Parasites
- Allergies
- Inflammation
- Neurogenic
Allergies in dogs

- 15-20% of dogs suffer from allergies
- Types of allergies
  - Parasites (esp. fleas)
  - Food
  - Environmental
    - Atopy
    - Contact
  - Drug
Atopic Dermatitis

- Affects 10-15% of dogs
- Pathogenesis
  - Genetics
  - Immunological
  - Structural
- Risk factors
  - Breed
  - Environment
  - Birthdate

Implications: not a homogenous disease—many factors involved
Genetics of Atopic Dermatitis

- Breeds predisposed
  - Terriers, setters, beagles, boxers, Lhaso Apso, pug, bulldogs, miniature schnauzer, retrievers, Dalmatian, GSD, others

- Breeding study (labs, retrievers)
  - 2 atopic parents: 65% offspring atopic
  - 1 atopic 1 normal: 57% offspring atopic
  - 2 normal parents: 11% offspring atopic

Implication – ideal not to breed affected dogs
Gene Mutations & AD

- Filaggrin
- Plakophilin 2
- SPINK5
- PPARγ
- IgA deficiency (GSD)
- Pro-inflammatory
  - S100A8
  - INPPL1
  - DPP4


Implications: not a homogenous disease, many targets for treatment, effectiveness of treatment may vary depending on cause in the individual dog
Skin Barrier Dysfunction in AD
Immunology of Atopy

- Allergen exposure
  - Predominantly percutaneous
  - Increased absorption of allergens in dogs with defective skin barrier function

- Antigen Processing Cells:
  - Langerhans cells and keratinocytes in skin
  - Present antigens to T-helper and B-cells to stimulate Ig production

- Sites of Ig production
  - Regional lymph nodes
Immunological Imbalances in Atopy

• Increased #s of dermal Langerhans cells
• Increase in T helper cells, predominantly Th2 cells
• Th2 cells preferentially induce B cells to produce IgE
• Th2 cells secrete IL-4, IL-5 and IL-10 which stimulate mast cells
• Importance: newer therapies target Th2 cells and cytokines produced by them
• Probiotics promote increase in Th1 cells
Antibodies in Atopic Dermatitis

- IgE bound to mast cells
- IgGd bound to mast cells
  - both can “trigger” mast cell degranulation following binding with allergen
- Importance = most in vitro assays were designed to detect only IgE and thus may not detect allergies in dogs with IgGd antibodies against allergens
- Not all dogs with “Atopic-Like Dermatitis” will have demonstrable allergen specific antibodies
Mast Cells & Skin Inflammation

Implication—many mediators, many targets for therapy!
Mediators of Inflammation

- IL-1 → lymphocyte activation
- IL-3 → T cell growth
- IL-4 → IgE production
- IL-5 → B cell growth, eosinophil activation
- IL-6 → fever
- IL-8 → chemotaxis (PMN)
- IL-13 → IgE production
- IL-31 → pruritus

Implication—many mediators = many targets for therapy!
Positive Feedback & Skin Inflammation

• Inflamed skin has disruption of permeability barrier and thus increased allergen absorption → greater inflammation → increased absorption → etc.

• AND inflamed skin has increased growth of bacteria and yeast → increased inflammation → increased growth of organisms

Implications for treatment targets
• Improve barrier function
• Alleviate inflammation
• Treat infections
Percutaneous Route of Allergen Exposure—practical applications

- Topical antihistamines, topical anesthetics, and topical CCS useful in decreasing inflammation

- Bathing atopic dogs is extremely important
  - removes surface allergens & organisms
  - delivers topical medications to skin
Clinical Signs

Pruritus
Erythema
  Alopecia
  Papules
  Excoriation
  Hyperpigmentation
  Lichenification
  Seborrhea
  Otitis
  Secondary infections
Morphological Distribution

- Face-muzzle, periocular
- Axillae
- Feet
- Flexor surface--elbow, tarsus
- Extensor surface--carpus
- Generalized in chronic cases

- Importance: major diagnostic criteria is lesion distribution
Associated Conditions

- Otitis
- Reverse sneezing, rhinitis
- “Hay Fever”, asthma
- Conjunctivitis
- Dry seborrhea
- Superficial pyoderma
- Sweating
Age of Onset of Clinical Signs

- 75% between 6 months and 3 years
- One study had 10% before 6 months and 34% by 9 months (Southern CA)
- Rare for onset > 7 years unless move to a new environment with new antigens
- Importance: a diagnostic criterion is age of onset
Seasonality for Atopy

- 78% begin in spring-fall
- 22% begin in winter
- 75% become year round
Allergenic Pollens

- Wind-pollinators
- Produce large amounts of pollen
- Sufficient numbers of plants present
- Pollen of size to be inhaled/absorbed
- Pollen that elicits IgE response
Highly Allergenic Pollens

• Trees
  • oaks, pecan, maples

• Grasses
  • timothy, orchard, red top, June (blue), sweet vernal, Johnson

• Weeds
  • ragweed, English plantain, lambsquarter, mugwort, March elder
Molds---Are Widespread

- **Alternaria**
  - saprophyte on plants and plant material
- **Hormodendrum (cladosporium)**
  - decaying materials
  - large #’s spores
- **Fusarium**
  - live and decaying plants
Molds---Are Widespread

- Aspergillus
  - soils
  - food
  - wet areas
- Helminthosporium (Botrytis)
  - grains
  - grasses
Molds---Are Widespread

- **Penicillium**
  - Soil, fruits, bread, cheeses

- **Mucor**
  - barns, animal wastes

- **Rhizopus**
  - plants, bread, cured meats, root vegetables
Molds---Are Widespread

- Phoma
  - paper products
- Pullularia
  - wet wood
- Curvularia
  - grasses
House Dust

- House Dust - contains many substances
  - bacteria, danders, fungi, insects & plant debris, food particles, mites
- Most important is Dermatophagoides
  - US -- farinae
  - Europe -- pteronyssinus
- Mite feces contain allergens, e.g., P1
  - up to 20 fecal particles/mite/day
House Dust Mites

• Feed on human epidermis
• Prefer 75-80% humidity & temperatures 25-30 C
• Most numerous in summer & fall
• Live in rugs, upholstered furniture, mattresses, also on birds and pets
• Become airborne with vacuuming
Other Environmentals

• Cotton linters
  • degeneration of fibrous materials

• Kapok
  • pillows, sleeping bags, life jackets, mattresses, cushions

• Cottonseed
  • mattresses, upholstery
Animal Allergens

• Cats
  • pelts, hair saliva, serum Ig’s
• Dogs
  • Serum Ig’s, dander
• Mouse/Rat
  • urine protein (males)
Animal Allergens

• Horse
  • Serum Ig’s, dander
• Cows
  • hair, dander, serum Ig’s
Insect Allergens

• Cockroaches
  • skin & eggs shells
• Apidae (honeybees)
  • PLA
• Fire ants
  • alkaloid in venom
Other Environmentals

• Sawdust/wood dust
• Feathers
• Human dander
• Storage mites (found in grain/cereal products including dry pet foods and many other substrates)
Diagnosis of Atopic Dermatitis

- Pruritus
- Typical morphology and distribution
  - Erythema
  - Symmetrical
  - Affecting ears, feet, face/muzzle, ventral abdomen, axilla and/or inguinal region
- Age of onset
  - 75% between 6 mo-3 yrs
- Chronic or relapsing

“a clinical syndrome”
Diagnosis of Atopic Dermatitis

- Rule out other causes of pruritus
  - Parasites
  - Food allergy
  - Contact dermatitis
  - Infections/inflammatory
  - Seborrheic dermatitis
  - Neurogenic

- Diagnostic aids
  - Elevated IgE levels (*D. farinae*)
  - Positive IDT
Diagnostic Criteria

• Major criteria

• Pruritus
  • Typical morphology & distribution
    • involving face &/or
    • feet &/or
    • legs
  • Seasonal or chronic dermatitis
  • Family or breed disposition
“Minor Criteria”

- Onset of symptoms < 3 years of age
- Facial erythema and cheilitis
- Bilateral conjunctivitis
- Superficial staphylococcal pyoderma
- Increased antigen-specific IgE
- Increased antigen-specific IgGd
- Immediate skin test reactivity
Must Also Rule These Out

• Ectoparasites
  • Fleas
  • Demodex
  • Sarcoptes

• Food Allergy

• Inflammation causing pruritus
  • Infections
  • Irritants
  • Dry Skin

• Neurogenic/Psychogenic
In Vitro Detection of Antigen Specific Serum IgE

- RAST
- ELISA
- Others
Pitfalls which Limit Usefulness

- Poor reproducibility
- Poor specificity for IgE
- Many false positives
  - non-specific binding
- Great seasonal variability
  - half-life of serum IgE = 2.5 days
- Not all reactions are IgE mediated (maybe also involve IgGd and type IV)
Pitfalls which Limit Usefulness

- No standardization
- Results vary between labs!
- Results vary within a lab! (study showed 60% repeatability)
- Results often do not correlate with pet’s exposure history
- HOWEVER some studies have shown good results to immunotherapy based on these tests
Intradermal Allergy Test

- Evaluates antigen-specific IgE and/or IgGd bound to mast cells in skin but not a perfect test (still have false + and false -)
- Can individualize test and test for more allergens than serum testing
- More specific – demonstrates allergens that cause inflammation in patient
Review important facts

- Atopic dermatitis affects 10-15% of dogs
- Many breeds are predisposed
- Age of onset is typically 6 mo to 3 yrs
- Clinical signs are an itch that rashes affecting the face, ears, feet, legs, axillary and inguinal regions
- Allergens are absorbed percutaneously
Review Important Facts

• Skin has biphasic T cell response
  • acute phase Th2 cells predominate
  • chronic Th1 cells increase

• Skin inflammation mediated by chemokines such as TNF-α, IL-1, IL-4, IL-5, IL-13, RANTES, eotaxin & others (many involved)
Review Important Facts

• Affected animals have cutaneous hyperactivity to environmental allergens

• Skin barrier dysfunction increases absorption of allergies and decreases resistance to secondary infections

• Reduced skin innate immune response augments susceptibility to infections
Review important facts

• Diagnosis is made by looking for major and minor criteria and ruling out other causes of pruritus
• ELISA, RAST, and IDAT are to be used to identify allergens for avoidance and for immunotherapy, not as a diagnostic test for atopy itself
• All of these tests have false –s and +s
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